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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/584,425 | 05/30/2007 | Tomoko Ono | 2352.014 | 1952 |
| 23405 | 7590 | 01/05/2011 | EXAMINER | |
| HESLIN ROTHENBERG FARLEY & MESITI PC 5 COLUMBIA CIRCLE ALBANY, NY 12203 | | | | GABEL, GAILENE |
| ART UNIT | | PAPER NUMBER | | |
| 1641 | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/584,425 | ONO ET AL. | |
| | Examiner | Art Unit | |
| | GAILENE R. GABEL | 1641 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 03 December 2010.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1,3 and 5-10 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1,3 and 5-10 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 3, 2010 has been entered.

Amendment Entry

2. Applicant's amendment and response filed December 3, 2010, is acknowledged and has been entered. Claims 1, 6, and 7-9 have been amended. Currently, claims 1, 3 and 5-10 are pending and are under examination.

Claim Rejections / Objections

3. All rejections or objections not reiterated herein have been withdrawn.

4. In light of Applicant's amendment, the scope of enablement rejection of claims 7-10 under 35 U.S.C. 112, first paragraph, is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 3, 5, and 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in reciting, "lower level" because the term "lower" is a subjective term lacking a comparative basis for defining its metes and bounds. Does Applicant intend that a slightly "lower" level of von Willebrand factor-cleaving protease encompassed in the claim provide increased severity of thrombophilia in the selected patient population? See also claim 7.

Claim 3 is indefinite in lacking antecedent basis in reciting, "the degree of thrombophilia."

Claim 7 is objected to in failing to further limit the claimed invention in reciting, "the bodily fluid is blood plasma."

Claim 8 is also objected to in failing to further limit the claimed invention in reciting, "diseases selected from the group consisting of pulmonary embolism, cerebral infarction, veno-occlusive disease, and deep vein thrombosis."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1, 3, and 5-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Scheiflinger et al. (US 2004/0214346 A1).

Scheiflinger et al. disclose a kit and diagnostic method for detecting and determining diagnosis of thrombosis manifested in a patient blood plasma sample by measuring the amount of von Willebrand factor-cleaving protease (vWF-cp) in the plasma sample [0015, 0029, 0032]. Thrombosis may be manifested in patients suffering from thrombotic microangiopathy (TM) [0034]. In practice, Scheiflinger et al. teach combining a blood sample from the patient with anti-vWFcp antibody that specifically binds to vWFcp immobilized into a solid phase and then detecting binding and complex formation of the anti-vWFcp antibody to vWFcp antigen using the immunological assay kit and method. The amount of vWFcp that bound to the anti-vWF antibody is also measured [0032]. Scheiflinger et al. show that a decrease in concentration of vWFcp in a patient in comparison to healthy control provides indication of occurrence of thrombosis ([0055, 0056]; Table 3).

As to the recitation of "severity of thrombophilia" it is well understood that "thrombophilia" or hypercoagulability is simply a measure of the propensity to develop or aggravate, i.e. degree of, thrombosis, and well-encompassed within the definition of thrombosis, because unpatented claims are given the broadest reasonable interpretation consistent with the specification.

Regarding the interpretive "wherein" clause recited in claims 3, 7, and 10 ("wherein the degree of thrombophilia is detected in a patient under a long term treatment with dialysis accompanied by repeated shunts" or [detected] in a person

under a long-term treatment with dialysis accompanied by repeated shunts), the clause does not recite any additional active method steps, but simply states a characterization or conclusion of the results of those steps. Therefore, the “wherein” clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. See *Texas Instruments, Inc. v. International Trade Comm.*, 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) (“A ‘whereby’ clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim.”). See also *Minton v. National Assoc. of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003) (“A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.”).

As to the application, i.e. intended use, of the claimed invention on patients suffering from the listed diseases in claim 1, it is deemed that the claimed method must result in a structural and functional difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. In this case, the severity of thrombophilia is being determined using a quantitative measure of vWFcp, regardless of the patient assay pool population.

7. Claims 1, 3, and 7-10 are rejected under 35 U.S.C. 102(a) as being inherently anticipated by Konetschny et al. (*Development of a Highly Sensitive and Specific Enzyme-linked Immunosorbent Assay for the Detection of ADAMTS-13 in Human*

Plasma, Blood 102 (11) Abstract #4062 (November 16, 2003)) in light of Scheiflinger et al. (US 2004/0214346 A1).

Konetschny et al. teach that von Willebrand factor (vWF) predominantly released from endothelial cells, when stimulated, are released as high molecular weight multimeric proteins having a large portion of unusually large vWF (ULVWF) which is hemostatically very active in efficiently interacting with platelet receptors and very effective in promoting platelet adhesion to sites of vascular injury. However, prolonged presence of hyperactive ULVWF leads to platelet aggregation and thrombus formation leading to thrombosis. Konetschny et al. teach a method of detecting occurrence of thrombosis in human plasma sample by measuring the amount of vWFcp present in the sample using highly sensitive and specific enzyme-linked immunosorbent assay (ELISA). vWF-cp (ADAMTS-13) is a metalloprotease discovered to actively regulate proteolytic degradation of ULVWF and that severe deficiency in vWFcp is also observed in acquired and hereditary TTP (1st full paragraph). In practice, Konetschny et al. teach immunologically measuring the amount of vWFcp that bound to the antibody by combining a blood sample from the patient with antibodies (anti-vWFcp) that specifically bind to vWFcp. Capture anti-vWFcp (anti-ADAMTS-13) polyclonal antibody is coated onto microtiter plate to capture vWFcp and detection anti-vWFcp MAb (242/H2) is conjugated to alkaline phosphatase so as to provide binding, detection, and measurement of vWFcp antigen present in the plasma (2nd full paragraph). Konetschny et al. show that a decrease in concentration of vWFcp manifested as a deficiency in

ADAMTS-13 in a patient in comparison to healthy control subject provides indication of occurrence of thrombosis (1st and 3rd full paragraphs).

As to the recitation of "severity of thrombophilia," it is well understood that "thrombophilia" or hypercoagulability is simply a measure of the propensity to develop or aggravate, i.e. degree of, thrombosis, and well-encompassed within the definition of thrombosis, because unpatented claims are given the broadest reasonable interpretation consistent with the specification.

As to recitation of thrombosis that is manifested in "patients suffering from diseases including pulmonary embolism, cerebral infarction, veno-occlusive disease, and deep vein thrombosis," Scheiflinger et al. discussed supra, indeed, teach that thrombosis as taught in the method of Konetschny et al. is manifested in patients suffering from cancer-associated TM in [0034]. Accordingly, it is deemed that Konetschny et al. inherently anticipates the claimed invention.

Regarding the interpretive "wherein" clause recited in claims 3, 7, and 10 ("wherein the degree of thrombophilia is detected in a patient under a long term treatment with dialysis accompanied by repeated shunts" or [detected] in a person under a long-term treatment with dialysis accompanied by repeated shunts), the clause does not recite any additional active method steps, but simply states a characterization or conclusion of the results of those steps. Therefore, the "wherein" clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. See Texas Instruments, Inc. v. International Trade Comm., 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) ("A 'whereby'

clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim.”). See also *Minton v. National Assoc. of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003) (“A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.”).

As to the application, i.e. intended use, of the claimed invention on patients suffering from the listed diseases in claim 1, it is deemed that the claimed method must result in a structural and functional difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. In this case, the severity of thrombophilia is being determined using a quantitative measure of vWFcp, regardless of the patient assay pool population.

Response to Arguments

8. Applicant's arguments with respect to claims 1 and 5-9 have been considered but are moot in view of the new grounds of rejection.

9. As to Applicant's argument regarding antibodies to vWFcp in the kit taught by Scheiflinger, it is maintained that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

December 17, 2010